UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/277,401	03/26/1999	MICHAEL JAYE	22,944-C USA	3515

7590 06/18/2004

GENE J. YAO, ESQUIRE
SYNNESTVEDT & LECHNER LP
2600 ARAMAK TOWER
1101 MARKET STREET
PHILADELPHIA, PA 19107

EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/277,401	JAYE ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16,22,44,57-59,63-65 and 98-105* is/are pending in the application.

4a) Of the above claim(s) *15,16,22,44,57,58,63-65 and 98-102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59 and 103-105* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on December 30, 2003), Applicants filed an election received on February 2, 2004. Claims 15, 16, 22, 44, 57-59, 63-65, and 98-105 are pending in the instant Office action.

Election

2. Applicant's election with traverse of Group VI, Claims 59 and 103-105, in the reply filed on February 2, 2004 is acknowledged. The traversal is on the ground(s) that the inventions are not independent. This is not found persuasive because the Patent Office holds that inventions that are independent OR distinct are distinctly patentable inventions, and the Examiner properly described why the different Groups were distinct, each from the other, in a previous Office action. Applicant also argues that to be searched together would not place undue burden on the Office. The Examiner disagrees based on the different class/subclasses that would require searching for all the noted inventions to be searched together.

The requirement is still deemed proper and is therefore made FINAL. Claims 15, 16, 22, 44, 57-59, 63-65, and 98-105 are pending. Claims 15, 16, 22, 44, 57, 58, 64-65, and 98-102 are withdrawn from further consideration as non-elected inventions. Claims 59 and 103-105 will be examined herein.

Priority

3. As previously noted, the instant application is granted the benefit of priority for the U.S. Provisional Application Nos. 60/032,254 and 60/032,783 filed on December 6, 1996 and U.S. non-Provisional Application No. 08/985,492 filed on December 5, 1997.

Drawings

4. The drawings are considered informal for the reasons detailed in the copy of PTO Form 948 attached to Paper No. 15 mailed on May 7, 2002. Appropriate correction is required in response to the instant Office action and **may not be held in abeyance** (see 37 C.F.R. § 1.85(a)).

Compliance with the Sequence Rules

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

a) The polynucleotide sequence in Figure 6 is not defined, either in the figure or in the brief description of the drawings.

If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the

same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Maintained - Objections to the Specification

6. Previous objection to the specification for being incomplete and confusing about the origin of the LIPG sequences and the SEQ ID NOs is maintained. Applicants have not effectively addressed this issue by amendment or argument. The following is repeated from the previous Office action for clarity.

From the original disclosure, SEQ ID NOs:1 and 2 are cDNA fragments of an LIPG identified by RT-PCR and SEQ ID NOs: 3 and 4 are cDNA fragments of an LIPG identified by 5'RACE extension analysis (see pages 20-21). These are human sequences as disclosed in the Examples (see pages 74-80). Then, SEQ ID NOs: 7 and 8 disclose the complete ORF of the human LIPG gene named LLGXL. Is this sequence related to fragments of SEQ ID NOs: 1-4? From the description added to page 25, it seems that SEQ ID NO:6 is a truncated version of SEQ ID NO:8, why the distinct name (SEQ ID NO:8 is called LLGXL and SEQ ID NO:6 is called LLGN)? Moreover, the role of SEQ ID NO:10 is wholly confusing. The Examiner suggests an overall description of the sequences in the listing; such a description could be added following the description of the figures. For clarity, such a description should include gene names, related polynucleotide/polypeptide sequences, and species sources; all this information must have clear support in the specification as originally filed.

7. Previous objection to the Abstract for not completely describing the disclosed subject matter is maintained. Applicants have not effectively addressed this issue by amendment or argument. The following is repeated from the previous Office action for clarity:

> "It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the **inclusion of the source species** of LIPG polypeptide, human and rabbit, for completeness." (emphasis added)

Correction is required.

New – Objections to the Specification

8. The amendment filed November 14, 2002 is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the five paragraphs inserted at page 25,between lines 7 and 8. Applicant describes said changes as "editorial in nature"; however, the language inserted must be supported elsewhere in the specification.

Applicant is required to cancel the new matter in the reply to this Office Action or to cite clear support (page and line number) for the amendment.

9. The specification is objected to for lacking updated continuity data in the first paragraph. The instant application claims the benefit of U.S. non-Provisional Application No. 08/985,492 filed on December 5, 1997, *now USPN 6,395,530.* Appropriate amendment to the specification is required (see M.P.E.P. § 201.11).

10. The specification is objected to for being confusing with respect to the sequence listing. The sequence listing contains 31 sequences. Every SEQ ID NO is mentioned in the specification and/or the claims except SEQ ID NOs: 5 and 9. It is unclear why said sequences are in the sequence listing if they are not described in the specification. All SEQ ID NOs in the sequence listing must be described in the specification. Appropriate correction is required.

11. The specification is objected to for not completely describing the following figures:

a) Figure 2 is disclosed has depicting SEQ ID NOs:1 and 2. While SEQ ID NO:1 is accurate, SEQ ID NO:2 is only the "coding region"; there is other amino acid sequence disclosed in the figure both 5' and 3' of the "coding region. All polypeptide sequence must be defined by SEQ ID NO.
b) Figure 3 is disclosed has depicting SEQ ID NOs:3 and 4. While SEQ ID NO:3 is accurate, SEQ ID NO:4 is only the "Coding region:5'RACE extension"; there is other amino acid sequence disclosed in the figure both 5' and 3' of the "coding region. All polypeptide sequence must be defined by SEQ ID NO.
c) Figure 13 depicts a rabbit LIPG PCR product (SEQ ID NO:11) and a fragment of SEQ ID NO:7; however, it is described as SEQ ID NO:7 which is confusing. Moreover, the numbering SEQ ID NO:7 is confusing since the figure does not disclose an N-terminal fragment (starting at nucleotide 1).

Clarification is required.

Previous Claim Objections/Rejections

12. All previous claim objections and rejections are herein withdrawn. In filing of the instant CPA, Applicant chose to change the invention being examined. Thus, all previously examined claims are withdrawn and/or cancelled rendering their objections/rejections moot.

Claim Rejections 35 U.S.C. § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 59 and 103-105 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "low" is a relative term. The term "low" in claim 59 is a relative term that renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Clarification is required.

14. Claims 59 and 103-105 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The abbreviation "LIPG" must be defined upon its first appearance in the claims for clarity. Applicant had previously argued, considering previously pending claim language, that the term "LIPG polypeptide" is a technical term clear to those skilled in the art referring to an endothelial lipase. If this is the case, the Examiner suggests replacing "LIPG polypeptide" with ---endothelial lipase (LIPG) polypeptide--- for clarity.

Additionally, the nature of an LIPG polypeptide (i.e., its structure) is ill defined in the specification. In the description of the figures, numerous LIPG polypeptides are defined. Their relationship to one another is unclear. Their source species are unclear. If they are full-length sequences is unclear, and does Claim 59 require identification of a full-length sequence? Does

this claim intend to identify SEQ ID NO:8 in a sample? From the disclosure, it seems that this might be the only full-length LIPG polypeptide disclosed. Clarification is required.

15. Claims 105 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear how measuring the level of LIPG mRNA accurately measures the amount of LIPG polypeptide. Translation of LIPG mRNA into LIPG protein is neither extricably linked nor quantitatively correlated by data in the instant specification. Clarification on the procedures using mRNA is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 59 and 103-105 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are directed to methods of identifying an LIPG polypeptide level in a sample from a patient. Since the term patient is not limited to human, any organism (with tissue) must be considered as a patient. Thus, any LIPG polypeptide must be able to be identified.

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

The specification teaches a single example of an LIPG polypeptide that is full-length, as expected to be found in a "patient", human. Identification of this species is fully described. However, the claims are not limited to this species. The genus of LIPG full-length polypeptides, and methods of identifying said polypeptides, lacks adequate written description because identifying characteristics of LIPG polypeptides have not been described so that one of skill in the art would be able to recognize other members of the claimed genus. The specification teaches the presence of a protein that interacts with the LIPG antibody disclosed therein in several mammalian species (see Figure 16); however, the nature of these polypeptides is unclear. Therefore, Claims 59 and 103-105, as written, fail to satisfy the written description requirement.

17. Claims 59 and 103-105 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods of identifying human LIPG levels in a human sample, does not reasonably provide enablement for methods of identifying the genus of LIPG levels in the genus of "patients". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To practice the full scope of the claimed methods would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The specification describes a single example of a full-length LIPG polypeptide such that it can be identified in a sample. While guidance is presented, both in the specification and the art, for identifying other LIPG polypeptides for identification in the claimed methods, one of skill in the art would be unable to "make" all, or a relevant portion of, the polypeptides within the scope of the claims because the ability to find an LIPG polypeptide (or gene encoding it) is not equivalent to the ability to make an LIPG polypeptide as required by the statute (i.e., "make and use"). No description in the specification or the art provides particular residues whose

encoding is important within the disclosed sequence so that its LIPG-nature is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. Therefore, the instant claims are not enabled to the full extent of their scope.

18. Claims 59 and 103-105 are rejected under 35 U.S.C. § 112, first paragraph, enablement, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To practice the claimed invention would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above.

The instant specification teaches that LIPG, overexpressed via an adenovirus in mice, reduces HDL cholesterol and apolipoprotein AI levels in said mouse (see page 110). The instant specification also teaches a 3 out of 4 correlation in atherosclerotic tissue for the presence of LIPG mRNA (see Example 10, pages 102-103). Neither of these results indicates that LIPG levels are necessarily predictive of HDL cholesterol and apolipoprotein AI levels. The transgenic mouse system is an artificial one producing levels of LIPG not supported by be naturally occurring. The atherosclerotic tissue system neither identifies LIPG polypeptide nor is 100% predictive. More recent studies of cardiovascular disease genes indicate that LIPG genetic variation does not correlate with cardiovascular disease (see Morabia *et al.* Human Molecular Genetics (2003) 12(21): 2733-2743, page 2740, Table 5 does not include the tested "EL"

protein). Thus, the data do not support the linkage of LIPG and HDL cholesterol or apolipoprotein AI needed to support the predictability of the claimed invention.

Other Relevant Art

19. The following are cited to complete the record:

a) Jaye *et al.* A novel endothelial-derived lipase that modulates HDL metabolism. Nature Genetics (1999) 21: 424-428.
b) Hirata *et al.* Cloning of a Unique Lipase from Endothelial Cells Extends the Lipase Gene Family (1999) 274(20): 14170-14175.

Conclusion

20. Claims 59 and 103-105 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Examiner
Art Unit 1652

June 15, 2004